ELSEVIER

Journal of Pharmaceutical and Biomedical Analysis
16 (1997) 529–532

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

Spectrophotometric determination of moclobemide by charge-transfer complexation

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Received 10 September 1996; received in revised form 26 March 1997

Abstract

A simple and sensitive spectrophotometric method is described for the assay of moclobemide. The method is based on the molecular interaction between the drug and chloranilic acid, to form a charge-transfer complex in which the drug acts as n-donor and chloranilic acid as π-acceptor. Chloranilic acid was found to form a charge-transfer complex in a 1:1 stoichiometry with a maximum absorption band at 526 nm. Conformity with Beer's law was evident over the concentration range 4–36 mg 100 ml^{-1}. A complete, detailed investigation of the complex formed was made with respect to its composition, association constant, molar absorptivity and free energy change. The method has been applied successfully to the analysis of commercially available moclobemide tablets with good recovery and reproducibility. © 1997 Elsevier Science B.V.

Keywords: Charge-transfer complexation; Chloranilic acid; Moclobemide; Spectrophotometric determination

1. Introduction

Moclobemide [*p*-chloro-*N*-(2-morpholinoethyl) benzamide] is a selective and reversible inhibitor of monoamine oxidase-type A (MAO-A) in man and the first benzamide antidepressant [1].

Charge-transfer complex-forming reactions have been used in the determination of electron-donating basic compounds through the interaction with σ(sigma)-acceptors [2,3] or π-acceptors [4–6]. As moclobemide contains a tertiary amino group in its molecular structure, it represents a basic centre with the availability of non-bonding electrons as donors. These facts encouraged the utilisation of the formation of complex between chloranilic acid and moclobemide for the determination of the drug in its tablet dosage form. This paper therefore reports the charge-transfer complex formation of moclobemide with chloranilic acid and its application to the drug assay. At the same time, the features of the complex such as the association constant, the molar absorptivity, the molar ratio of reaction and the free energy change (ΔG^0) were determined.

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PII S0731-7085(97)00086-1

2. Experimental

2.1. Materials and reagents

Aurorix® tablet (Roche, Nigeria), chloranilic acid (Riedel de Haen), dioxan and chloroform (May and Baker, Nigeria) were used. Other reagents and solvents were analytical grade and used as such. All laboratory reagents were freshly prepared.

2.2. Absorption spectra

A solution of chloranilic acid (5×10^{-3} M) was made in 1,4-dioxan and its wavelength of maximum absorption was determined using a digital Milton Roy, Spectronic 1201. A colour was developed by mixing 2 ml of chloranilic acid with 2 ml of 3×10^{-3} M moclobemide and the wavelength of maximum absorption for the resulting solution was determined.

2.3. Standard curve

For calibration, a 300 mg portion of moclobemide base was weighed accurately in an analytical balance (Sartorius) and dissolved in 100 ml of anhydrous chloroform. Serial concentrations of 0.3–3.6 mg in 0.3 mg steps of standard base solution were transferred to different test tubes. Sufficient chloroform was added to bring the volumes to 3 ml and 2 ml of chloranilic acid (3×10^{-2} M) in dioxan was added to bring the volumes to 5 ml. The contents were mixed and left at room temperature for 30 min after which their absorbance was measured at 526 nm against a blank, prepared simultaneously without moclobemide solution.

2.4. Assay procedure for tablets

An amount of pulverised Aurorix® tablets equivalent to 300 mg of moclobemide was transferred to a 100 ml flask with the aid of chloroform and shaken for 30 min to dissolve the drug. The solution was then filtered to remove the excipients and the filtrate made up to 100 ml mark with chloroform. Serial volumes of 0.1–0.6 ml in 0.1 ml steps of the solution were transferred to different test tubes and sufficient chloroform was added to bring the volumes to 3 ml. A total 2 ml of (3×10^{-2} M) chloranilic acid in dioxan was added to each reaction mixture to bring the volume to 5 ml and then proceeded as described in Section 2.3.

2.5. Stoichiometric relationship

Master solutions of equimolar concentrations (3.72×10^{-3} M) of moclobemide and chloranilic acid were prepared. A series of 5 ml quantities of mixtures of the master solutions comprising complementary proportions of the two solutions (0.5:4.5; 1.0:4.0; …4.5:0.5) were transferred to different test tubes and the complex formed for each reaction mixture allowed to stand for 30 min before analysis at 526 nm.

2.6. Association constant and free energy change

Serial volumes of 0.4–2.4 ml of 10^{-2} M moclobemide solution in 0.4 ml steps were transferred into different test tubes. The solution was diluted with chloroform to 3 ml, and 1.0 ml of 5×10^{-3} M chloranilic acid in dioxan was added. The procedure was continued as described for the calibration of moclobemide.

3. Results and discussion

The immediate change of the yellowish-pink colour of chloranilic acid in dioxan to purple upon reaction with moclobemide was suggestive of charge-transfer complex formation. This change in colour further justified scanning in the visible region of the spectrum. The purple chromogen given by moclobemide with chloranilic acid exhibited a strong absorption maximum at 526 nm, while chloranilic acid absorbed maximally at 430 nm (Fig. 1). This band can be attributed to the formation of charge-transfer complex between moclobemide, acting as n-donor (D) or Lewis base, and chloranilic acid as the π-acceptor (A) or Lewis acid according to Scheme 1 with the subsequent formation of a coloured anion radical of chloranilic acid.

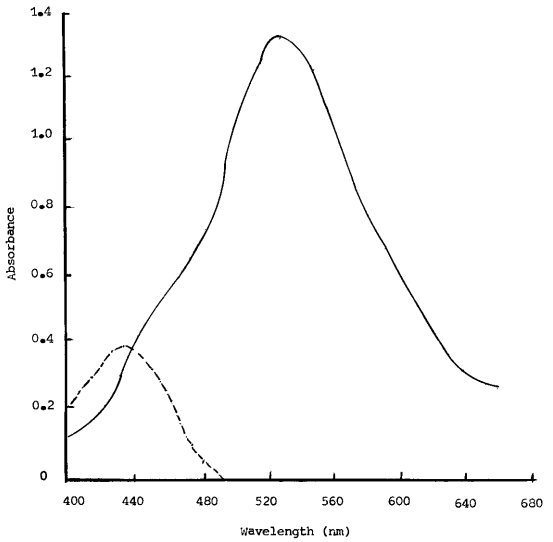

Fig. 1. Absorption spectra of chloranilic acid (– · –) and moclobemide chloranilic acid complex (——). Chloranilic acid: 5×10^{-3} M; molcobemide: 3×10^{-3} M.

Although the complex was formed rapidly, constant absorbance readings were obtained only after no less than 30 min at room temperature (Table 1). The readings, however, remained constant for at least another 90 min with the purple colour still retained even after 24 h of storage in the dark but with marked reduction in the absorbance values.

Application of Job's method of continuous variation [7] indicated a 1:1 complexation ratio (Fig. 2). This finding was anticipated because of the presence of one strong basic or electron-donating centre in the moclobemide structure. The absorbance of the moclobemide–chloranilic acid complex was used to calculate the association constant using the Benesi–Hildebrand equation [8] which depends on the experimental condition that one of the two component species should be present in large excess, so that its concentration is virtually unaltered on formation of a complex.

$$\ddot{D} + A \longrightarrow [\ddot{D} \curvearrowright A] \longrightarrow D^+ + A^-$$

(outer complex) (inner complex)

Scheme 1.

Table 1
Effect of time on absorbance of moclobemide–chloranilic acid complex

Minutes after mixing	Absorbance at 526 nm
0	0.500
30	0.590
60	0.590
90	0.590
120	0.589
150	0.580
180	0.581
210	0.578

Using the method of least squares [9], the regression equation describing the line obtained from the Benesi–Hildebrand plot for the formed complex is:

$$\frac{[A_0]}{A_\lambda^{AD}} = 1.144 \times 10^{-3} + \frac{1}{[D_0]}(1.24 \times 10^{-6}) \qquad (1)$$

for which the regression coefficient equals 0.9499. From Eq. (1), the association constant equals 922.214 l mol^{-1} and the molar absorptivity equals 874.409 mol l^{-1}. The standard free energy change [10] of complexation was related to the association constant and calculated to be -4.11 kcal.

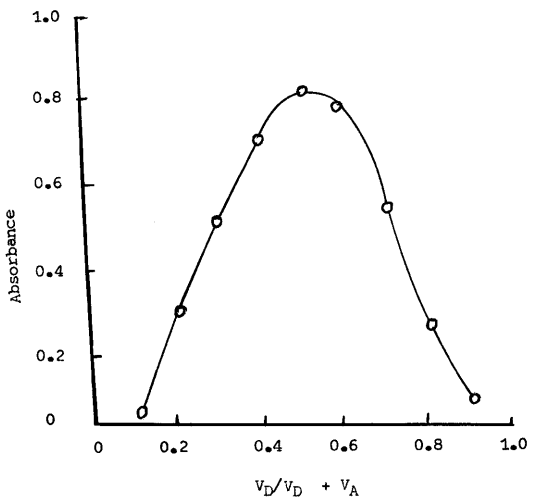

Fig. 2. Job's plot for moclobemide–chloranilic acid complex: 3.73×10^{-3} M.

Table 2
Assay results for moclobemide in its dosage form

Aurorix® tablets (150 mg tab^{-1})[a]	Recovery (%)
A	100.75
B	100.58
C	99.48
D	100.50
E	98.47
F	100.89
Mean	100.11
Standard deviation	±0.95
Calculated value of t[b]	0.28

[a] According to label claim.
[b] The value for t-theoretical at $\propto = 0.05$ is 2.015.

The standard calibration graph for moclobemide was constructed by plotting absorbance versus concentration (mg 100 ml^{-1}) calculated after the addition of the chloranilic acid solution. Conformity with Beer's law was evident in the concentration range 4–36 mg 100 ml^{-1}. The regression equation derived using the method of least squares is:

$$A_{526} = 1.93 \times 10^{-3} + 2.39 \times 10^{-2}C \quad (2)$$

for which the regression coefficient is 0.9999. A_{256} is the absorbance at 526 nm, and C is the concentration of moclobemide expressed in mg 100 ml^{-1}. Deviations from linearity in Beer's plot result when the concentrations of donor and acceptor differ in magnitude [11] with a consequent formation of termolecular complexes. For this reason, the concentration of chloranilic acid solution was kept slightly higher than, but at the same order of magnitude as, that of the moclobemide.

The validity of the regression equation was assessed in the determination of moclobemide in Aurorix® tablets. Table 2 shows the accuracy of the proposed method.

Recovery experiments carried out on six different Aurorix® tablets show high quantitative recoveries with low standard deviation. The performance of the proposed method was judged through calculation of the Student's t-value. At the 95% confidence level, the calculated value of t does not exceed the theoretical value. This indicates that the proposed method gives results not significantly different from the true values according to label claims and further confirms the high accuracy of the method. Compared to most official methods, the proposed method is simpler, faster and more sensitive, and gives good recoveries. These advantages encourage its application in the analysis and quality control of drugs. Other drugs with basic centres are expected to give similar chromophores. Amino acids and proteins also give sensitive responses with π-acceptors [12].

References

[1] The Power to Lift Depression, A Profile on Moclobemide, Hoffman-La Roche, Basel, Switzerland, 1995, 636-901-223.
[2] H.S.I. Tan, E.D. Gerlach, A.S. Dimattio, J.Pharm. Sci. 66 (1977) 766.
[3] A.F.M. El Walily, A. El Gindy, A.A.M. Wahbi, J. Pharm. Biomed. Anal. 13 (1995) 53.
[4] S. Belal, M.A. Elsayed, M.E. Abdel-Hamid, H. Abdine, J. Pharm. Sci. 70 (1981) 127.
[5] H. Abdel, M.A.-H. Elsayed, I. Chaaban, M.E. Abdel-Hamid, Analyst 103 (1978) 1227.
[6] M.S. Rizk, M.I. Walash, F.A. Ibrahim, Analyst 106 (1981) 1163.
[7] R. Rose, Advanced Physico-chemical Experiments, Pitman, London, 1964, p. 54.
[8] H.A. Benesi, J.H. Hildebrand, J. Am. Chem. Soc. 71 (1949) 2703.
[9] E.L. Bauer, Statistical Manual for Chemists, Academic Press, London, 1971, p. 61.
[10] A.N. Martin, J. Swarbrick, A. Cammarata, Physical Pharmacy, 2nd ed., Lea and Febiger, Philadephia, PA, 1969, pp. 343, 360.
[11] R. Foster, Organic Charge-Transfer Complexes, Academic Press, London, 1969, p. 171.
[12] F. Alsulimany, A. Townshend, Anal. Chim. Acta 66 (1973) 195.